

Comparison of Probability Curves Obtained from 2 Quantitative Allergen-specific IgE Assays: FEIA and 3gAllergy™

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Abstract: The validity and benefit of probability curves in allergen-specific IgE (sIgE) testing and their applicability to more than a few allergens are still pending. One study^[1] presented probability curves for 4 food allergens and proposed decision points to rule out the need for food challenges in his clinic. Since then, such cutoffs were reported by Boyano-Martinez^[2] to be dependent on population, age, allergen and disease. A recent article by Söderström^[3] extended the use of probability curves to 8 inhalant allergens. The results were allergen dependent and site specific. None of the studies, however, has addressed the potential impact of IgE specific for cross-reacting carbohydrate determinants (CCD) on these probability curves^[4]. In this study, we use logistic regression model to compare the probability curves for food and inhalant allergens using two quantitative sIgE assays; an FEIA (Pharmacia CAP) and DPC's automated chemiluminescent IMMULITE® 2000. The FEIA yields explicit results down to 0.35 kU L⁻¹; the "third-generation" IMMULITE 2000 has an analytical sensitivity of 0.1 kU L⁻¹ and provides precise quantification down to 0.2 kU L⁻¹. In previous studies^[6,7], patients with suspected IgE-mediated allergy were evaluated according to skin prick tests or food challenges positive or negative allergen-specific diagnosis. Logistic regression was performed using the online regression analysis facility at: <http://members.aol.com/johnp71/logistic.html>, which is part of the Interactive Statistical Calculations web site. For inhalant allergens, almost identical overall probability curves were obtained for the FEIA and IMMULITE 2000 methods. For food allergen, similar probability curves were obtained with the two methods. The probability curves were allergen dependent. The FEIA and IMMULITE 2000 methods gave similar allergen-dependent profiles, however and in one case (W6), both methods yielded identical probability curves. The present study demonstrates that the 2 sIgE assays yield comparable probability curves for the inhalant and food allergens tested. Because the FEIA method is unable to yield explicit results below 0.35 kU L⁻¹, the probability curve generated is necessarily truncated at this level. Methods for sIgE measurement that allow for extending probability curves below 0.35 kU L⁻¹ can also assess assay performance more definitively at the traditional 0.35 kU L⁻¹ cutoff. Thus the third-generation IMMULITE 2000 is a better tool for defining probability curves, as the applicability of such curves in allergy testing and the potential impact of IgE to CCD become well understood.

Key words: Fluorescent enzyme immunoassay, IMMULITE® 2000 THIRD Generation Allergen-specific IgE, logistic regression, odds ratios, probability curves

INTRODUCTION

Sampson^[1] presented probability curves for four food allergens and proposed decision points, which could be used to eliminate the need for double-blind, placebo-controlled food challenges in his clinic. In his report, the curves illustrate graphically that even a low concentration of food-specific IgE antibodies might be associated with a risk of clinical reactivity. Since then, other investigators^[2] have concluded that cutoff levels, however, depended on population, age, allergens and diseases. Söderström *et al.*^[3] extended the concept of probability curves to inhalant allergens. His study on eight allergens evaluated at four separate clinics deals with the question whether high risk was associated with

higher levels of sIgE and whether quantitative results were more useful than qualitative (positive/negative) determinations. He speculated that the concept of probability for an allergic reaction or positive clinical allergy conclusion would be a better diagnostic tool compared with the traditional qualitative measures including class correlation. None of the studies, however, has addressed the potential impact of IgE specific for cross-reacting carbohydrate determinants (CCD) on these probability curves^[4].

The Söderström study^[3] has led to many unanswered questions^[5]. The implications of obtaining different probability curves among different clinics for the same allergens are not clear. Factors affecting the shapes of the curves are also not entirely known or

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explained. For instance, why are the curves for D1 and E1 so different at the four clinics?

In previous studies^[6,7], patients with suspected IgE-mediated allergy were evaluated according to skin prick tests and food challenges, respectively. The objective of our study was to apply the logistic regression model in order to compare the probability curves for one food (F2), two insects (I1 and I3) and seven inhalant (D1, D2, E1, G3, G6, T3 and W6) allergens, obtained from two quantitative sIgE methodologies: FEIA and IMMULITE 2000 Third Generation, (3gAllergy).

MATERIALS AND METHODS

Logistic regression was performed using the online regression analysis facility at: <http://members.aol.com/johnp71/logistic.html>, which is part of the Interactive Statistical Calculations web site.

For the two insects and seven inhalant allergens, we used skin prick tests^[6] in clinic 1 as the true status. For F2, we used food challenges in clinic 2^[7] as the true status. The same blood samples were subject to FEIA and 3gAllergy analysis.

RESULTS

In the study performed at clinic 1, almost identical overall probability curves (Fig. 1) were obtained for the FEIA and 3gAllergy methodologies, using the two insects and seven inhalant allergens with N=766 results. Overall model fit gave Chi Square of 308.4 and 253.0, respectively with df=1 and p= 0.0001.

Table 1: Comparison of odds ratios between the 2 methodologies

Odds Ratios	FEIA	Immulate 2000	Difference
D1	1.0575	1.0738	0.0163
W6	2.2821	2.2489	0.0332
ALL	1.2964	1.1829	0.1135
E1	1.1856	1.0566	0.129
D2	1.8879	1.6615	0.2264
F2	1.4072	1.1047	0.3025
G6	1.7076	1.2677	0.4399
G3	1.7202	1.2015	0.5187
I3	2.6032	2.0257	0.5775
I1	1.1359	3.4914	2.3555
T3	2.0204	4.582	2.5616

For the F2 food allergen study done in clinic 2, similar F2 probability curves (Fig. 2) were obtained for the FEIA and 3gAllergy methodologies: N=31 results. Overall model fit gave Chi Square of 19.1 and 17.1, respectively with df=1 and p= 0.0001.

In agreement with Söderström's report^[3], probability curves are allergen dependent. The two FEIA and 3gAllergy methodologies, however gave similar allergen dependent profiles (Fig. 3 and 4). With certain allergens, the 2 methodologies can yield identical (W6) probability curves (Fig. 5).

According to Gallagher^[8], a positive ratio of 1 to 2 alters disease probability by a small and clinically

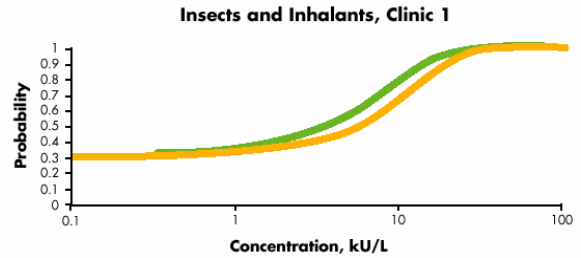


Fig. 1: Probability of receiving positive diagnosis at a given sIgE concentration for the 9 insect and inhalant allergens at clinic 1. Blue denotes FEIA methodology and magenta denotes 3gAllergy methodology

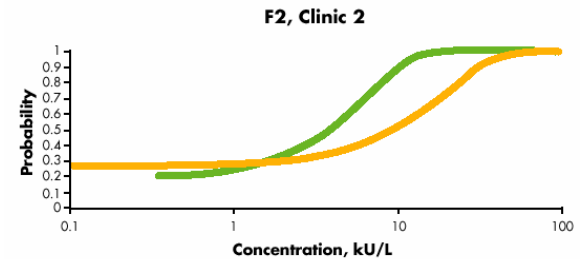


Fig. 2: Probability of receiving positive diagnosis at a given sIgE concentration for the F2 cow's milk allergen at clinic 2. Blue denotes FEIA methodology and magenta denotes 3gAllergy methodology

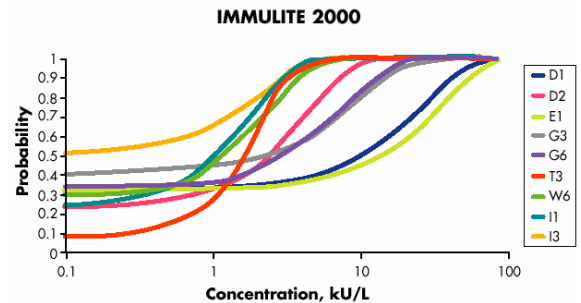


Fig. 3: Probability of receiving positive diagnosis at a given sIgE concentration for D1, D2, E1, G3, G6, T3, W6, I1 and I3 allergen at clinic 1 using the 3gAllergy methodology

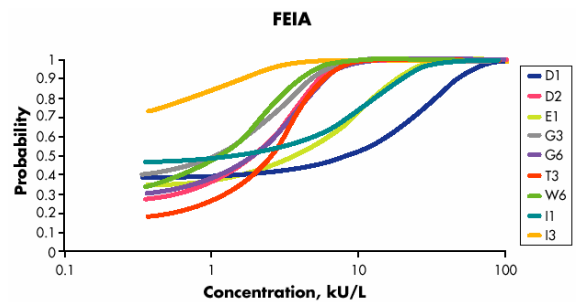


Fig. 4: Probability of receiving positive diagnosis at a given sIgE concentration for D1, D2, E1, G3, G6, T3, W6, I1 and I3 allergen at clinic 1 using the FEIA methodology

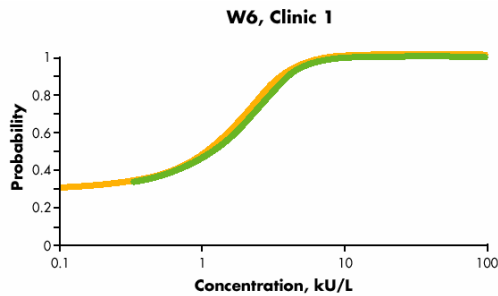


Fig. 5: Probability of receiving positive diagnosis at a given sIgE concentration for the W6 allergen at clinic 1. Blue denotes FEIA methodology and magenta denotes 3gAllergy methodology

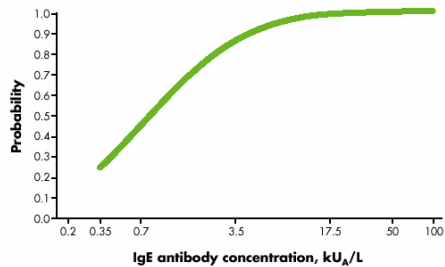


Fig. 6: From Soderstrom (2003) with permission from Blackwell Publishing: Theoretical probability curve of probability to show symptoms as a function of sIgE concentration

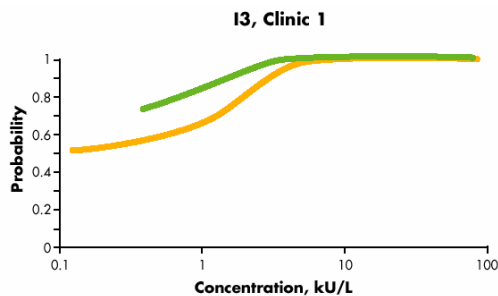


Fig. 7: Probability of receiving positive diagnosis at a given sIgE concentration for the I3 allergen at clinic 1. Blue denotes FEIA methodology and magenta denotes 3gAllergy methodology

insignificant degree. Positive ratios greater than 10 may have substantial impact on clinical decision making through meaningful revision of disease probability. Table 1 indicates there are no significant differences in the odds ratios among all of the 10 allergens evaluated.

CONCLUSION

This study demonstrates that probability curves for the two insects, seven inhalant allergens and one food allergen generated via two quantitative sIgE assays are comparable. The FEIA and 3gAllergy probability curves give odds ratios that differ by no clinical significance.

Because the FEIA methodology uses 0.35 kU L^{-1} as cut off, the probability curve generated begins at 0.35 kU L^{-1} (Fig. 6). Söderström^[3] commented that different slopes and intercepts in probability curves may indicate different identification patterns of symptoms; a steep curve would indicate symptoms easily linked to an allergen even with low levels of IgE antibodies. A more flat curve in contrast, would indicate a difficulty to link even high levels of IgE antibodies as the trigger of the symptoms. Probability curves extending below 0.35 can provide a more complete curve profile (the I3 probability curves in Fig. 7) and can be useful for the assessment of the true slope and intercept. Thus the 3gAllergy methodology which provides precise quantification down to 0.2 kU L^{-1} [9,10] can offer a better tool in defining the probability curve profile.

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